

applicants submit that claims 60 and 61 are properly grouped with the claims of Group I. Further, applicants submit that the amendments made to the claims in this paper further serve to unify claims 60 and 61 with the claims of Group I.

Accordingly, applicants believe it is proper to begin prosecution of Group I wherein Group I is defined as comprising the following claims: 1-43, 49-51, 53, 54, 56-59, 60-62, 64 and 65.

2. Amendment

In the Claims:

Please cancel claims 9-20, 23, 30-33, 37-48, 50-55, 57, 59, 61, 63, and 65-67, without prejudice or disclaimer. Please amend claims 1-3, 5-8, 21, 22, 24-28, 36, 49, 58, 60, 62, and 64, without prejudice or disclaimer, as shown in Appendix A. Please add new claims 68-86 as shown in Appendix A. A clean copy of the pending claims after entry of this paper is presented in Appendix B.

The pending claims after entry of this amendment are claims 1-8, 21, 22, 24-29, 34-36, 49, 56, 58, 60, 62, 64 and 68-86.

Remarks

Cancellation or amendment of the claims has been made without prejudice or disclaimer. Applicants expressly reserve the right to bring the subject matter of the original claims again in a subsequent, related application.

Support for the amendments to claim 1 may be found throughout the specification as originally filed, for example, at the following locations: originally presented claims 9, 13, 14, and 15; page 3, line 20, to page 4, line 1; page 24, lines 9-13; page 20, lines 4-5; and page 20, lines 26-30.

Support for the amendments to claim 2 may be found throughout the specification as originally filed, for example, at the following location: Figure 1.

Support for the amendments to claim 3 may be found throughout the specification as originally filed, for example, at the following locations: page 3, lines 9-10; and page 24, lines 30-31.

Support for the amendments to claim 5 may be found throughout the specification as originally filed, for example, at the following location: page 3, line 15.

Support for the amendments to claims 6-8 may be found throughout the specification as originally filed, for example, at the following location: page 3, lines 14-19.

Support for the amendments to claim 21 may be found throughout the specification as originally filed, for example, at the following locations: originally presented claims 1, 9, 13, 14, and 15;; page 3, line 20, to page 4, line 1; page 24, lines 9-13; page 20, lines 4-5; and page 20, lines 26-30.

Support for the amendments to claim 22 may be found throughout the specification as originally filed, for example, at the following locations: originally presented claims 1 and 3.

Support for the amendments to claims 24-28 may be found throughout the specification as originally filed, for example, at the following locations: originally presented claim 1; Figure 1; and page 4, lines 10-25.

Claim 36 was amended to provide correct claim dependency.

Claim 49 was amended to remove unnecessary the terms from the claim.

Support for the amendments to claims 58 and 60 may be found throughout the specification as originally filed, for example, at the following locations: originally presented claim 58; page 23, lines 12-20; page 2, lines 24-26; and page 18, lines 25-30.

Support for the amendments to claim 62 may be found throughout the specification as originally filed, for example, at the following locations: originally presented claims 1, 3, 64, and 65.

Support for the amendments to claim 64 may be found throughout the specification as originally filed, for example, at the following location: originally presented

claim 65.

Basis for newly presented claims 68 and 69 may be found throughout the specification as originally filed, for example, at the following locations: originally presented claims 1, 9, 13, 14, and 15.

Basis for newly presented claim 70 may be found throughout the specification as originally filed, for example, at the following location: originally presented claim 34.

Basis for newly presented claim 71 may be found throughout the specification as originally filed, for example, at the following location: originally presented claim 35.

Basis for newly presented claim 72 may be found throughout the specification as originally filed, for example, at the following location: originally presented claim 36.

Basis for newly presented claim 73 may be found throughout the specification as originally filed, for example, at the following location: originally presented claim 49.

Basis for newly presented claim 74 may be found throughout the specification as originally filed, for example, at the following locations: originally presented claims 64 and 65.

Basis for newly presented claims 75 and 76 may be found throughout the specification as originally filed, for example, at the following location: page 22, lines 19-23.

Basis for newly presented claim 77 may be found throughout the specification as originally filed, for example, at the following location: originally presented claim 56.

Basis for newly presented claim 78 may be found throughout the specification as originally filed, for example, at the following locations: page 32, lines 5-16; and page 23, line 23, to page 24, line 13.

Basis for newly presented claims 79-86 may be found throughout the specification as originally filed, for example, at the following locations: originally presented claims 58-61; page 23, lines 12-20; page 2, lines 24-26; page 18, lines 25-30; page 32, lines 5-16; and page 23, line 23, to page 24, line 13.

Accordingly, no new matter has been added by way of this amendment and the entry thereof is respectfully requested.

CONCLUSION

Applicants expressly reserve their right under 35 U.S.C. §121 to file one or more divisional applications directed to the non-elected subject matter during the pendency of this application. Upon allowance of generic claims, applicants request consideration of claims to additional species which are written in dependent form or which otherwise include all the limitations of the allowed generic claims.

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any matters that may be facilitated by a telephone interview, applicants request that the Examiner contact the undersigned at the telephone number given below.

Please direct all further communications in this application to:

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Respectfully submitted,

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APPENDIX B

APPENDIX A

Marked-up copy of the claims as amended herein.

1. (Amended) An expression cassette comprising,
a polynucleotide encoding *luxA*, *luxB*, *luxC*, *luxD* and *luxE* gene products,
5 wherein (a) [the arrangement of coding sequences for the gene products is in the
following relative order 5' - *luxA-luxB-luxC-luxD-luxE*- 3'; (b)] transcription of the
polynucleotide results in a polycistronic RNA encoding all the gene products; [and (c)]
(b) each of the *luxA*, *luxB*, *luxC*, *luxD* and *luxE* gene products is expressed as an
individual polypeptide; and (c) polynucleotide sequences comprising Gram-positive
10 ribosome-binding site sequences are located 5' to all of said *lux* coding sequences.
2. (Amended) The expression cassette of claim 1, [wherein] further comprising a
multiple-insertion site [is] located [adjacent the] 5' [end of the] to said *luxA*, *luxB*, *luxC*,
luxD and *luxE* coding sequences.
- 15 3. (Amended) The expression cassette of claim 1, [further comprising] wherein
at least one Gram-positive ribosome binding site comprises the sequence presented as
[(]SEQ ID NO:1[)] upstream of each of the polynucleotide sequences encoding each of
the *luxA*, *luxB*, *luxC*, *luxD* and *luxE* gene products].
- 20 4. The expression cassette of claim 1, wherein the coding sequences of the gene
products are derived from *Photobacterium luminescens*.
5. (Amended) The expression cassette of claim 1[5], wherein [transcription of]
25 the polynucleotide [is mediated by] further comprises a promoter [contained in an
Expression Enhancing Sequence selected from the group consisting of Sa1-Sa6] located
5' to all of said *lux* coding sequences wherein transcription of the polynucleotide results
in a polycistronic RNA encoding all the *lux* gene products.

6. (Amended) The expression cassette of claim 5, wherein [transcription of the polynucleotide is mediated by a] said promoter is contained in an Expression Enhancing Sequence selected from the group consisting of [Sa2 and Sa4] Sa1, Sa2, Sa3, Sa4, Sa5, and Sa6.

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7. (Amended) The expression cassette of claim [1] 5, wherein [transcription of the polynucleotide is mediated by a] said promoter is contained in an Expression Enhancing Sequence selected from the group consisting of Sp1, Sp5, Sp6, Sp9, Sp16 and Sp17.

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8. (Amended) The expression cassette of claim 7, wherein [transcription of the polynucleotide is mediated by a] said promoter is contained in Expression Enhancing Sequence Sp16.

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9. (Canceled) *An expression cassette comprising, a polynucleotide encoding luxA, and luxB gene products, wherein (a) transcription of the polynucleotide results in a polycistronic RNA encoding both gene products, and (b) polynucleotide sequences comprising Gram-positive ribosome-binding site sequences are located adjacent the 5' end of the luxA coding sequences and adjacent the 5' end of the luxB coding sequences.*

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10. (Canceled) *The expression cassette of claim 9, further comprising an insertion site 5' to at least one of either the luxA or luxB coding sequences.*

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11. (Canceled) *The expression cassette of claim 10, wherein the insertion site further comprises a multiple-insertion site.*

12. (Canceled) *The expression cassette of claim 11, wherein the multiple-insertion site is located 5' to the luxA coding sequences.*

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13. (Canceled) *The expression cassette of claim 9, wherein said polynucleotide further encodes luxC, luxD and luxE gene products.*

14. (Canceled) *The expression cassette of claim 12, wherein the arrangement of coding sequences for the lux gene products is in the following relative order 5' - luxA-luxB-luxC-luxD-luxE- 3'.*

15. (Canceled) *The expression cassette of claim 12, wherein Gram-positive bacterial Shine-Dalgarno sequences are 5' to all of said lux coding sequences.*

16. (Canceled) *The expression cassette of claim 12, wherein transcription of the polynucleotide is mediated by a promoter contained in an Expression Enhancing Sequence selected from the group consisting of Sa1-Sa6.*

17. (Canceled) *The expression cassette of claim 16, wherein transcription of the polynucleotide is mediated by a promoter contained in an Expression Enhancing Sequence selected from the group consisting of Sa2 and Sa4.*

18. (Canceled) *The expression cassette of claim 12, wherein transcription of the polynucleotide is mediated by a promoter contained in an Expression Enhancing Sequence selected from the group consisting of Sp1, Sp5, Sp6, Sp9, Sp16 and Sp17.*

19. (Canceled) *The expression cassette of claim 18, wherein transcription of the polynucleotide is mediated by a promoter contained in Expression Enhancing Sequence Sp16.*

20. (Canceled) *The expression cassette of claim 9, wherein the coding sequences for luxA and luxB are obtained from Photorhadus luminescens.*

21. (Amended) *An expression cassette comprising,*

a polynucleotide encoding *luxA*, *luxB*, and *luc* gene products, wherein (a) transcription of the polynucleotide results in a polycistronic RNA encoding all three gene products, [and] (b) polynucleotide sequences comprising Gram-positive [bacterial Shine-Dalgarno] ribosome-binding site sequences are located adjacent the 5' end of the *luxA* coding sequences, adjacent the 5' end of the *luxB* coding sequences, and adjacent the 5' end of the *luc* coding sequences, and (c) each of the *luxA*, *luxB*, and *luc* gene products is expressed as an individual polypeptide.

22. (Amended) The expression cassette of claim 21, wherein said polynucleotide further encodes *luxC*, *luxD* and *luxE* gene products, wherein (i) Gram-positive ribosome-binding site sequences are located 5' to each of the *luxC*, *luxD*, and *luxE* coding sequences, and (ii) each of the *luxC*, *luxD*, and *luxE* gene products is expressed as an individual polypeptide.

23. (Canceled) *The expression cassette of claim 22, wherein Gram-positive bacterial Shine-Dalgarno sequences are located 5' to all of the lux coding sequences.*

24. (Amended) The expression cassette of claim 21, wherein [transcription of] the polynucleotide [is mediated by] further comprises a promoter [contained in an Expression Enhancing Sequence selected from the group consisting of Sa1-Sa6] located 5' to all of said *lux* and *luc* coding sequences wherein transcription of the polynucleotide results in a polycistronic RNA encoding all the *lux* and *luc* gene products.

25. (Amended) The expression cassette of claim 24, wherein [transcription of the polynucleotide is mediated by a] said promoter is contained in an Expression Enhancing Sequence selected from the group consisting of [Sa2 and Sa4] Sa1, Sa2, Sa3, Sa4, Sa5, and Sa6.

26. (Amended) The expression cassette of claim [21] 24, wherein [transcription of the polynucleotide is mediated by a] said promoter is contained in an Expression

Enhancing Sequence selected from the group consisting of Sp1, Sp5, Sp6, Sp9, Sp16 and Sp17.

27. (Amended) The expression cassette of claim 26, wherein [transcription of the
5 polynucleotide is mediated by a] said promoter is contained in Expression Enhancing
Sequence Sp16.

28. (Amended) The expression cassette of claim 21, [wherein] further
comprising a multiple-insertion site [is] located [adjacent the] 5' [end of the] to said *luxA*,
10 *luxB*, *luxC*, *luxD* and *luxE* coding sequences.

29. The expression cassette of claim 21, wherein the coding sequences for *luxA*
and *luxB* are obtained from *Photorhadus luminescens*.

15 30. (Canceled) *An expression cassette comprising,*
a polynucleotide encoding an in-frame fusion of luxA and luxB gene products,
wherein (a) polynucleotide sequences comprising Gram-positive Shine-Dalgarno
sequences are located adjacent the 5' end of the luxA coding sequences, and (b) an
insertion site is located between the luxA and luxB coding sequences.

20 31. (Canceled) *The expression cassette of claim 30, wherein the insertion site*
further comprises a multiple-insertion site.

25 32. (Canceled) *The expression cassette of claim 30, wherein said polynucleotide*
further encodes luxC, luxD and luxE gene products, wherein the arrangement of coding
sequences for the gene products is in the following relative order 5' - luxA/luxB-luxC-
luxD-luxE- 3'

33. (Canceled) *The expression cassette of claim 32, wherein Gram-positive bacterial Shine-Dalgarno sequences are 5' to the luxA/luxB fusion coding sequences and all of the luxC, luxD, and luxE coding sequences.*

5 34. The expression cassette of claim 1, wherein the expression cassette is contained within a bacterial transposon.

35. The expression cassette of claim 1, wherein the expression cassette is contained within a bacterial mini-transposon.

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36. (Amended) The expression cassette of claim [34] 1, wherein the coding sequences of the gene products comprise codons that are optimal for expression of the gene products in a host system into which the expression cassette is to be introduced.

15 37. (Canceled) *A method of selecting a light-producing expression cassette for use in a selected cell type, said method comprising*
preparing fragments of genomic DNA isolated from the selected cell type,
inserting the fragments into the insertion site of an expression cassette of any of
claims 30, where the expression cassette is capable of expressing the gene products in the
20 *selected cell type,*
introducing the expression cassettes carrying the fragments into cells of the
selected cell type, and
screening for cells producing light, where said light production is mediated by the
expression cassette.

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38. (Canceled) *The method of claim 37, where said fragments are produced by enzymatic digestion of genomic DNA.*

39. (Canceled) *The method of claim 38, where said fragments are produced by*
30 *partial digestion using a selected restriction endonuclease.*

40. (Canceled) *The method of claim 37, where said fragments are produced by mechanical fragmentation of the genomic DNA.*

5 41. (Canceled) *The method of claim 37, wherein transcription of the lux genes is mediated by a promoter that is obtained from the selected cell type.*

42. (Canceled) *The method of claim 37, wherein the selected cell type is selected from the group consisting of Staphylococcus, Streptococcus, Actinomyces, Lactobacillus, Corynebacterium, Mycobacterium, Clostridium, Propionibacterium, Enterococcus, and Bacillus.*

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43. (Canceled) *The method of claim 37, where said screening is carried out at a temperature greater than 37°C.*

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44. (Canceled) *A luciferase expression cassette comprising:*
a) a polynucleotide encoding luc; and
b) polynucleotide sequences comprising expression enhancing sequences obtained from Gram-positive bacteria 5' to said luc-encoding polynucleotide.

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45. (Canceled) *The expression cassette of claim 44 wherein the expression enhancing sequences are Gram-positive Shine-Dalgarno sequences.*

46. (Canceled) *The expression cassette of either of claim 44 wherein the expression enhancing sequences are Gram-positive promoter sequences.*

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47. (Canceled) *The expression cassette of claim 44, wherein the small DNA fragment is between luc and the promoter and wherein the small DNA fragment is selected from the group consisting of a nucleotide encoding an open-reading frame of the iron transport protein of Stapholococcus a polynucleotide encoding an open-reading*

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frame of the alanine-racine operon and a polynucleotide encoding an open-reading frame a protein having homology to a Bacillus protein.

48. (Canceled) The plasmids designated pCMOR G+1 Sal-6 and pCMOR G+2
5 Sp1, Sp5, Sp6, Sp9, Sp16 and Sp17.

49. (Amended) A shuttle vector comprising:
[a)] an expression cassette according to claim 1;
[b)] a polynucleotide encoding a selectable marker;
10 [c)] a Gram-positive origin of replication; and
[d)] a Gram-negative origin of replication.

50. (Canceled) A method of screening for expression enhancing sequences that are useful in obtaining expression of luciferase in Gram-positive bacteria, comprising:
15 a) introducing DNA fragments from a Gram-positive bacterial genome into an expression cassette comprising (i) polynucleotides encoding luxA, luxB, luxC, luxD and luxE gene products, where the polynucleotides are in the following relative order 5' - luxABCDE; (ii) polynucleotide sequences comprising expression enhancing sequences obtained from Gram-positive bacteria 5' to at least one of said lux-encoding
20 polynucleotides and (iii) an insertion site 5' to at least one of said lux-encoding polynucleotides;
b) transforming the expression cassette of step (a) into a Gram-positive bacteria host cells; and
c) determining the level of luciferase activity in the host cell, thereby identifying
25 Gram-positive expression enhancing DNA sequences that are useful in obtaining expression of luciferase in Gram-positive bacteria.

51. (Canceled) A method of screening for expression enhancing sequences that are useful in obtaining expression of luciferase in Gram-positive bacteria, comprising:

- 5 a) introducing DNA fragments from a Gram-positive bacterial genome into an expression cassette comprising (i) polynucleotides encoding luxA, luxB gene products (ii) polynucleotide sequences comprising expression enhancing sequences obtained from Gram-positive bacteria 5' to at least one of said lux-encoding polynucleotides and (iii) an insertion site 5' to at least one of said lux-encoding polynucleotides;
- b) transforming the expression cassette of step (a) into a Gram-positive bacteria host cells; and
- 10 c) determining the level of luciferase activity in the host cell, thereby identifying Gram-positive expression enhancing DNA sequences that are useful in obtaining expression of luciferase in Gram-positive bacteria.

52. (Canceled) A method of screening for expression enhancing sequences that are useful in obtaining expression of luciferase in Gram-positive bacteria, comprising:
- 15 a) introducing DNA fragments from a Gram-positive bacterial genome into an expression cassette comprising (i) a polynucleotide encoding luc; (ii) polynucleotide sequences comprising expression enhancing sequences obtained from Gram-positive bacteria 5' to said luc-encoding polynucleotide and (iii) an insertion site 5' to at least one of said luc-encoding polynucleotide;
- 20 b) transforming the expression cassette of step (a) into a Gram-positive bacteria host cells; and
- c) determining the level of luciferase activity in the host cell, thereby identifying Gram-positive expression enhancing DNA sequences that are useful in obtaining expression of luciferase in Gram-positive bacteria.

- 25 53. (Canceled) A method of making a luciferase expression cassette, comprising the steps of:
- (a) preparing polynucleotides encoding in a 5'-3' direction luxA, luxB, luxC, luxD and luxE gene products; and Gram-positive Shine-Dalgarno nucleotide sequences operably linked to one or more of said lux-encoding polynucleotides; and

(b) *inserting small sequences of nucleic acids between one or more of the polynucleotides encoding a lux gene product.*

5 54. (Canceled) *A method of making a luciferase expression cassette, comprising the steps of:*

(a) *preparing polynucleotides encoding luxA and luxB gene products; and Gram-positive Shine-Dalgarno nucleotide sequences operably linked to one or more of said lux-encoding polynucleotides; and*

10 (b) *inserting small sequences of nucleic acids between one or more of the polynucleotides encoding a lux gene product.*

55. (Canceled) *A method of making a luciferase expression cassette, comprising the steps of:*

15 (a) *preparing polynucleotides encoding luc gene product; and Gram-positive Shine-Dalgarno nucleotide sequences operably linked to said luc-encoding polynucleotide; and*

(b) *inserting small sequences of nucleic acids 5' to said luc-encoding polynucleotide.*

20 56. *A method of modifying a Gram-positive organism to produce light, comprising transforming the Gram-positive organism with an expression cassette according to claim 1.*

25 57. (Canceled) *The method of claim 56 further comprising providing, if necessary, the substrate required for luciferase activity.*

58. (Amended) *A method of screening an analyte for its ability to affect expression of a reporter marker, comprising:*

30 [(a) *transforming Gram-positive bacteria with a luciferase expression cassette according to claim 4;*]

[(b)] providing the analyte to [the bacteria] Gram-positive bacteria comprising the luciferase expression cassette of claim 1, wherein said reporter marker comprises luciferase; and

5 [(c) providing, if necessary, the substrate required for luciferase light production; and]

[(d)] monitoring the effect of the analyte on the ability of the Gram-positive bacteria to produce light, thereby identifying whether the analyte affects expression of the reporter in Gram-positive bacteria.

10 59. (Canceled) The method of claim 58, wherein the substrate is aldehyde and is provided as a vapor.

60. (Amended) A method of screening an analyte for its ability to affect expression of a reporter marker in a [whole] living, non-human animal, comprising:

15 [(a) transforming Gram-positive bacteria with a luciferase expression cassette according to claim 1;]

[(b)] introducing Gram-positive bacteria comprising the luciferase expression cassette of claim 1 into [a whole] the animal, wherein said reporter marker comprises luciferase;

20 [(c)] providing the analyte to the animal; and

[(d) providing, if necessary, the substrate required for luciferase light production; and]

25 [(e)] monitoring the effect of the analyte on the ability of the Gram-positive bacteria to produce light, thereby identifying whether the analyte affects expression of the reporter in Gram-positive bacteria in the living, non-human animal.

61. (Canceled) The method of claim 60, wherein the substrate is aldehyde and is provided by injection.

62. (Amended) A Gram-positive bacteria capable of producing light, wherein (a) the bacteria comprises luxA, [and] luxB, luxC, luxD, and luxE coding sequences, and (b) about 1×10^6 bacterial cells can produce at least about 1×10^4 Relative Light Units at about 37°C.

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63. (Canceled) *A transgenic non-human animal comprising an expression cassette according to claim 1.*

64. (Amended) A Gram-positive bacteria comprising an expression cassette
10 according to claim 1.

65. (Canceled) *The bacteria according to claim 64, wherein the bacteria is gram-positive.*

15 66. (Canceled) *A bacteria comprising a plasmid according to claim 48.*

67. (Canceled) *The bacteria according to claim 66, wherein the bacteria is gram-positive.*

20 68. (NEW) The expression cassette of claim 1, wherein the arrangement of the coding sequences for the *lux* gene products is in the following relative order 5' - *luxA-luxB-luxC-luxD-luxE*- 3'.

25 69. (NEW) The expression cassette of claim 21, wherein the arrangement of the coding sequences for the *lux* gene products is in the following relative order 5' - *luxA-luxB-luxC-luxD-luxE*- 3'.

70. (NEW) The expression cassette of claim 21, wherein the expression cassette is contained within a bacterial transposon.

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71. (NEW) The expression cassette of claim 21, wherein the expression cassette is contained within a bacterial mini-transposon.

5 72. (NEW) The expression cassette of claim 21, wherein the coding sequences of the gene products comprise codons that are optimal for expression of the gene products in a host system into which the expression cassette is to be introduced.

10 73. (NEW) A shuttle vector comprising:
an expression cassette according to claim 21;
a polynucleotide encoding a selectable marker;
a Gram-positive origin of replication; and
a Gram-negative origin of replication.

15 74. (NEW) A Gram-positive bacteria comprising an expression cassette according to claim 21.

75. (NEW) A bacteria comprising the vector of claim 49.

20 76. (NEW) A bacteria comprising the vector of claim 73.

77. (NEW) A method of modifying a Gram-positive organism to produce light, comprising transforming the Gram-positive organism with an expression cassette according to claim 21.

25 78. (NEW) The method of claim 77 further comprising providing the substrate required for *luc*-mediated luciferase activity.

79. (NEW) A method of screening an analyte for its ability to affect expression of a reporter marker, comprising:

providing the analyte to Gram-positive bacteria comprising the luciferase expression cassette of claim 21, wherein said reporter marker comprises luciferase;

providing substrate required for luciferase light production; and

5 monitoring the effect of the analyte on the ability of the Gram-positive bacteria to produce light, thereby identifying whether the analyte affects expression of the reporter in Gram-positive bacteria.

80. (NEW) The method of claim 79, wherein said substrate is aldehyde and is provided as a vapor.

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81. (NEW) The method of claim 79, wherein said substrate is a substrate for the *luc* gene product.

82. (NEW) The method of claim 79, wherein said substrate is (i) aldehyde and is provided as a vapor, and (ii) a substrate for the *luc* gene product.

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83. (NEW) A method of screening an analyte for its ability to affect expression of a reporter marker in a living, non-human animal, comprising:

20 introducing Gram-positive bacteria comprising the luciferase expression cassette of claim 21 into the animal, wherein said reporter marker comprises luciferase;

providing the analyte to the animal;

providing substrate required for luciferase light production; and

25 monitoring the effect of the analyte on the ability of the Gram-positive bacteria to produce light, thereby identifying whether the analyte affects expression of the reporter in Gram-positive bacteria in the living, non-human animal.

84. (NEW) The method of claim 83, wherein said substrate is aldehyde and is provided by injection.

85. (NEW) The method of claim 83, wherein said substrate is a substrate for the *luc* gene product and is provided by injection.

86. (NEW) The method of claim 83, wherein said substrate is (i) aldehyde and is
5 provided as a vapor, and (ii) a substrate for the *luc* gene product.

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